

THE EFFICACY OF HALOXON AND THIABENDAZOLE AS ANTHELMINTICS AGAINST GASTRO-INTESTINAL NEMATODES IN SHEEP

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INTRODUCTION

Since many species of parasitic nematodes are picked up by the host grazing on contaminated pastures, control measures are generally directed towards proper range or pasture management as well as towards an appropriate animal husbandry program. In most areas where severe parasitism occurs, livestock owners must treat their animals several times each year with anthelmintic drugs in order to keep the animals as free of parasites as possible. Some of the problems which relate to drug treatment are not only the cost of the drugs and of handling the livestock several times each year, but also the fact that drug resistant strains of parasites frequently develop to routinely-used drugs.

Examination, in the fall of 1967, of the sheep kept at the BYU Research Farm at Provo, Utah, indicated that gastro-intestinal parasitism by certain nematodes could represent a serious problem. One yearling lamb died as a result of natural infection of the large stomach worm of sheep, *Haemonchus contortus*, on 22 September, 1967. This lamb had a count of 5,200 eggs per gram (e.p.g.) of feces, and exhibited other symptoms of haemonchosis, including edema of the head and thoracic and abdominal cavities. Other lambs killed on different experiments at this same approximate time also had several hundred *H. contortus* adults in the abomasum.

Since all of the sheep at the farm had been treated routinely during the past eight years with low levels of phenothiazine mixed in the feed, we decided to test the anthelmintic efficacy of Thiabendazole* and Haloxon**, two drugs which had not been used previously at the BYU Research Farm.

PROCEDURE AND RESULTS

On 30 September, 1967, we obtained fecal samples from 107 sheep maintained at the farm. Some of these sheep had been on

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*Thiabendazole is an imidazole derivative with the chemical formula of 2-(4-thiazolyl)-benzimidazole, and a product of Merck and Company, Rahway, New Jersey.

**Haloxon is an organophosphate compound with the chemical formula of O,O-di(2-chloroethyl) O-(3-chloro-4-methylconmarin-7-yl) phosphate, and a product of William Cooper and Nephews, Inc., Chicago, Illinois.

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irrigated grass pasture during the entire summer, while others had been used on nutrition experiments, and had been held on drylot only. Those on drylot had only small numbers of eggs or none in the feces. Of those held on pasture, we were able to identify 25 adult sheep that had egg counts varying from 200 to 3500 trichostrongylid eggs per gram of feces. For the purpose of the experiment, these sheep were divided into three groups on the basis of the egg count. Group A, consisting of 8 sheep, had an average e.p.g. of 1028 (range: 200 to 2100) and on 19 October, 1967, each animal was given, by dose syringe, 1 fluid ounce of Thiabendazole mixture, containing 2 gm Thiabendazole per fluid ounce. Group B, consisting of 9 sheep, had an average e.p.g. of 1230 (range: 200 to 3500) and on 19 October, 1967, each animal received 1 fluid ounce of Haloxon containing 1.4 gm Haloxon per fluid ounce. Drug dosages were based on manufacturers' recommendations. Group C, consisting of 8 sheep, which had an average e.p.g. of 1300 (range: 200 to 3400) served as the control group. Fecal samples were collected again 12 days after treatment was given. At that time the average e.p.g. in Group A (Thiabendazole-treated) had dropped to 8 (range: 0 to 100), a 99% reduction in total egg count, Group B (Haloxon-treated) had dropped to 19 (range: 0 to 100), a 98% reduction, and the control sheep had also dropped to an average e.p.g. of 275 (range: 0 to 900), a 79% reduction. The average e.p.g. counts for all three groups of sheep prior to and 12 days after treatment are listed in Table 1.

In order to determine which genera of nematodes were affected by the drugs, larval cultures were made from all fecal samples from the 25 sheep prior to and after treatment. Table II shows the numbers of larvae examined and their assignment to various genera, based on the tables prepared for total length and sheath tail length by Dikmans and Andrews (1933) and Keith (1953). Our ranges of total and sheath tail measurements differed slightly from the tables we were using, but the identification of *Haemonchus*, *Chabertia*, *Ostertagia*, *Trichostrongylus*, and *Nematodirus* was considered valid.

From the results we obtained, it was noted that Thiabendazole was highly effective against *Trichostrongylus* and *Ostertagia*, since no larvae of these genera were detected after treatment. The percent of *Haemonchus* larvae constituted 67% of the larvae identified before treatment and 27% of those identified after treatment. The percentage of *Chabertia* larvae increased from 4% prior to treatment to 47% after treatment, and the percentage of *Cooperia* rose from 7% to 20%. Haloxon appeared completely effective in eliminating *Haemonchus*, *Cooperia* and *Ostertagia*, but not as effective against *Trichostrongylus* as was Thiabendazole. The percentage of *Trichostrongylus* in the Haloxon-treated group increased from 14% prior to treatment to 21% after treatment, *Oesophagostomum* rose from 2% to 5%, and 68% of all larvae identified after treatment from the Haloxon-treated group were identified as *Chabertia*,

TABLE I
Effect of anthelmintics on gastro-intestinal nematodes of sheep

Group #	No. of Sheep	Mean No. nematode eggs per gram feces before treatment	Treatment	Mean No. nematode eggs per gram feces after treatment
A	8	1028	1 fl. oz. Thiabendazole per sheep	8
B	9	1230	1 fl. oz. Haloxon per sheep	19
C	8	1300	Controls—no treatment	275

TABLE II
Gastro-intestinal nematode larvae identified in fecal cultures from sheep treated with anthelmintics

Group #	No. of Sheep	No. larvae identified before treatment	Percentages of larvae before treatment*						No. larvae identified after treatment	Percentages of larvae after treatment								
			Ha.	Tr.	Oc.	Ch.	Co.	Os.		Ne.	Un.	Tr.	Oc.	Ch.	Co.	Os.	Ne.	Un.
A	8	96	67	10	..	4	7	3	..	9	15	27	..	47	20	6
B	9	87	76	14	3	5	19	..	21	6	68	5
C	8	96	68	14	..	5	3	6	79	39	27	3	6	18	5	2

- *Ha. = Haemonchus
- Tr. = Trichostrongylus
- Oc. = Oesophagostomum
- Ch. = Chabertia
- Co. = Cooperia
- Os. = Ostertagia
- Ne. = Nematodirus
- Un. = Unidentified

whereas none had been identified in that group prior to treatment. The most significant change in the percentages of the various genera in the control sheep was a decrease in *Haemonchus* from 68% prior to the time the two groups were treated, to 39% when the control sheep were sampled afterwards. The percentages of larvae identified as *Trichostrongylus* and *Cooperia* showed corresponding increases during this period.

DISCUSSION AND CONCLUSIONS

Although the variation in nematode egg counts was considerably greater than would have existed had we infected the sheep experimentally with equal numbers of infective larvae, this project, nevertheless, showed that both Thiabendazole and Haloxon are effective anthelmintics against the majority of gastro-intestinal nematodes encountered. It was unfortunate, however, that the problem was identified and started so late in the pasture season, since the marked drop in egg counts in the control sheep undoubtedly related to decreased numbers of infective larvae being picked up by the grazing sheep at that time of the year. *Haemonchus contortus* larvae in particular are highly susceptible to colder temperatures as demonstrated by the seasonal e.p.g. decline in the control animals, and generally do not develop from the egg to the infective larval stage at mean monthly temperatures of less than 65° F, or when the total monthly rainfall is less than 2 inches per month (Levine, 1963; Kates, 1965). The mean monthly temperatures in a standard weather shelter in Provo for June, July, August, September, and October, 1967, were 62.3, 73.3, 72.3, 62.6, and 47.9 F respectively. The total precipitation for those five months was 1.26, 0.96, 0.16, 0.77, and 0.55 inches, respectively. Therefore, the conditions for the development and survival of the free-living stages of *Haemonchus*, as far as available moisture was concerned, would appear to be considerably less than optimum for these months. The precipitation for these months in 1967 did not differ markedly from the long-term averages for Provo for the four main pasture months of June, July, August, and September, since these are all less than 1 inch per month. During this same period, however, farmers in this area put as much water on their lands through irrigation as that comparable to 20 inches of rainfall. Some of the lowland pastures are frequently completely saturated by irrigation water that may be allowed to run for several days in any one pasture location. These conditions of moisture, coupled with the fact that the soil temperature measurements may actually be 15-20° F higher than that recorded in a standard weather shelter (Andersen and Levine, 1967) certainly are capable of producing micro-environmental conditions optimum for the development and survival of these nematode larvae. Nevertheless, when the project herein reported was conducted during the late pasture season, the number of larvae available on the pasture would naturally be decreasing

due to low temperatures. On the 13th and 14th of September the minimum daily temperatures in the weather shelter were only 29 and 32° F, respectively, and 6 of the 16 remaining days in September had minimum temperatures less than 40° F. These low temperatures, undoubtedly, would decrease the numbers of viable larvae on the pasture, thereby resulting in fewer new infections in the grazing sheep. Had the total egg counts from the control sheep remained at the same approximate level as that before treatment, the efficacy of the two anthelmintics tested would have been much clearer.

Since the numbers of larvae recovered from fecal samples following treatment was very limited in the two treated groups, the comparison of the effect of the drugs on the specific genera as determined by larval identification must be interpreted provisionally. No more than 100 eggs per gram of feces was noted in any of the treated sheep. With such small numbers, the recovery of sufficient numbers of larvae for identification after laboratory culture is very difficult, and only a total of 34 infective larvae were identified from these two treated groups. Nevertheless, as mentioned above, the identification of most of the genera was considered valid. Infective *Haemonchus contortus* larvae are particularly easy to identify and the fact that none of these were found in any fecal samples taken from the Haloxon-treated sheep seemed quite significant.

As stated above, one of the main difficulties in using continual chemotherapy as a control measure in parasitism is the frequent development of strains of the parasites resistant to the chemicals being used. Phenothiazine, for example, was first introduced as an anthelmintic in swine by Harwood, Jerstad and Swanson in 1938, and then by a number of authors in 1939 (See Gibson, 1965) as an anthelmintic in sheep. Early reports showed this drug to be 75-90% effective against *Haemonchus* when used in crude preparations, and later up to 100% effective when used in a micronized-powder form. Strains of *Haemonchus* resistant to phenothiazine were first reported in 1957 in Kentucky by Drudge, Leland, and Wyant, and later noted by such authors as Enzie *et al.* (1960) in Maine, and Levine and Garrigus (1961) in Illinois. In the latter case, phenothiazine had been used routinely at the sheep division at the University of Illinois for 19 years before the resistant strain was identified.

Thiabendazole was first introduced as an anthelmintic in sheep by Brown *et al.* in 1961. This drug proved to be an extremely effective broad-spectrum anthelmintic and has been used widely in many geographical locations for treatment of parasitic helminths. Efficacy against *Haemonchus* in sheep ranged as high as 96-100% (Hebden, 1961; Gordon, 1961). Since that time, however, strain resistance has appeared against this drug also. Smeal *et al.* (1968) recently reviewed accounts of resistance to Thiabendazole that have been noted in the United States and Brazil, as well as the work

they reported on for Australia. Since 27% of the larvae recovered after treatment in the Thiabendazole-treated animals in our project were *Haemonchus*, there is at least some suggestion that the *Haemonchus* in this geographical area are also somewhat resistant to this drug. Since the drug has not been used at the BYU Research Farm, however, such a conclusion would imply that resistant strains have been brought to this area by sheep that have been purchased elsewhere.

The efficacy of Thiabendazole against parasitic helminths has been reported in several hundred scientific articles, and annotated bibliographies are available on this subject from Merck and Company, Inc., Rahway, New Jersey. Haloxon has not been tested as widely in the United States, but its efficacy against several genera of gastro-intestinal nematodes in sheep as well-documented by such authors as Armour, Brown and Sloan (1962), Harbour (1963), Barnett, Berger, and Rodrigues (1964), Turk, Galvin and Bell (1965), and Baker and Douglas (1965). In general, these workers found Haloxon to be a highly efficacious anthelmintic against most of the same genera of parasitic nematodes as was Thiabendazole, with the exception that it was not as effective against such genera as *Chabertia*, the large-mouthed bowel-worm, or *Oesophagostomum*, the large intestinal nodular worm. Haloxon is apparently hydrolyzed before it reaches the large intestine, and is therefore more effective against nematodes which occur in the abomasum and small intestine. We also found that Haloxon was not effective against *Chabertia* and *Oesophagostomum*, although as stated earlier, the small numbers of larvae identified suggests that this conclusion be interpreted provisionally.

Although comparative studies on the efficacy of phenothiazine were not included in this project, the fact that the animals had been treated routinely with phenothiazine for the past eight years, and yet the fact that severe haemonchosis can occur here, also suggests that strains resistant to this drug exist in this area. Experiments involving critical testing where worm counts and speciations can be made at necropsy after treatment with Thiabendazole, Haloxon, and phenothiazine should be conducted, before the problem of possible resistant strains in this area can be resolved.

REFERENCES

- ANDERSEN, F. L., AND N. D. LEVINE. 1967. Methods and problems in micro-environmental measurements. III. *Vet.* 10:10-17.
- ARMOUR, J., P. R. M. BROWN, AND J. E. N. SLOAN. 1962. The anthelmintic efficacy of haloxon against the adult and immature stages of gastro-intestinal nematodes. *Vet. Rec.* 74:1454-1457.
- BARNETT, S. F., J. BERGER, AND C. RODRIGUES. 1964. A small controlled trial of the anthelmintics haloxon and thiabendazole in sheep. *Afr. Agr. For. J.* 29:195-198.
- BAKER, N. F., AND J. R. DOUGLAS. 1965. Anthelmintic activity of haloxon in lambs. *Am. J. Vet. Res.* 26:651-653.

- BROWN, H. D., A. R. MATZUK, I. R. ILVES, L. H. PETERSON, S. A. HARRIS, L. H. SARETT, J. R. EGERTON, J. J. YAKSTIS, W. C. CAMPBELL, AND A. C. CUCKLER. 1961. Antiparasitic drugs. IV. 2-(4'-thiazolyl)-benzimidazole, a new anthelmintic. *J. Am. Chem. Soc.* 83:1764-1765.
- DIKMANS, G. AND J. S. ANDREWS. 1933. A comparative morphological study of the infective larvae of the common nematodes parasitic in the alimentary tract of sheep. *Tr. Am. Micr. Soc.* 52:1-25.
- DRUDGE, J. H., S. E. LELAND, JR., AND Z. N. WYANT. 1957. Strain variation in the response of sheep nematodes to action of phenothiazine. II. Studies on pure infections of *Haemonchus contortus*. *Am. J. Vet. Res.* 18:317-325.
- ENZIE, F. D., M. L. COLGLAZIER, G. E. WHITMORE, AND D. E. THOMPSON. 1960. Effectiveness of three management systems on parasitism in lambs. III. Resistance of *Haemonchus contortus* to phenothiazine. *J. Parasit.* 46 (suppl.): 41.
- GIBSON, T. E. 1965. Veterinary Anthelmintic Medication. Technical Communication No. 33 of the Commonwealth Bureau of Helminthology. St. Albans, Herts. 206 pages.
- GORDON, H. McL. 1961. Thiabendazole; a highly effective anthelmintic for sheep. *Nature* 191:1409-1410.
- HARBOUR, H. E. 1963. Experience with organo-phosphorus compounds as anthelmintics. *Internat. Vet. Cong.* pp. 751-756.
- HARWOOD, P. D., A. C. JERSTAD, AND L. E. SWANSON. 1938. The efficacy of phenothiazine for the removal of ascarids and nodular worms from swine. *J. Parasit.* 24:16-17.
- HEBDEN, S. P. 1961. The anthelmintic activity of thiabendazole (MK-360). *Austral. Vet. J.* 37:264-269.
- KATES, K. C. 1965. Ecological aspects of helminth transmission in domesticated animals. *Am. Zool.* 5:95-130.
- KEITH, R. K. 1953. The differentiation of the infective larvae of some common nematode parasites of cattle. *Austral. J. Zool.* 1:223-235.
- LEVINE, N. D. 1963. Weather, climate, and the bionomics of ruminant nematode larvae. *Adv. Vet. Sci.* 8:215-261.
- LEVINE, N. D., AND U. S. GARRIGUS. 1961. The effect of Cu-Nic and organo-phosphorus anthelmintics on phenothiazine-resistant *Haemonchus* in sheep. *Am. J. Vet. Res.* 23:489-493.
- SMEAL, M. G., P. A. GOUGH, A. R. JACKSON, AND I. K. HOTSON. 1968. The occurrence of strains of *Haemonchus contortus* resistant to thiabendazole. *Austral. Vet. J.* 44:108-109.
- TURK, R. D., T. J. GALVIN, AND R. R. BELL. 1965. Comparative tests of the anthelmintics haloxon, phenothiazine and thiabendazole in sheep and goats. *Southwest. Vet.* 19:44-47.